CLAIMS

WHAT IS CLAIMED IS:

1. A method of detecting the presence or absence of a first posttranslational modification of a plurality of proteins in a sample, the method comprising:

providing the sample comprising the proteins;

providing a pooled population of a plurality of subsets of particles, the particles in each subset comprising a capture reagent specific for at least one of the proteins, and the particles in each subset being distinguishable from those of every other subset;

providing a single first detection reagent, the first detection reagent providing an indication of the presence of the first posttranslational modification;

binding the proteins to the capture reagents;

exposing the proteins to the first detection reagent; and,

determining whether each of the proteins comprises the first posttranslational modification by identifying each subset of particles and detecting the presence or absence of the first detection reagent on each subset of particles.

2. The method of claim **1**, wherein the particles in each subset comprise a capture reagent specific for one of the proteins.

3. The method of claim **1**, wherein binding the proteins to the capture reagents comprises exposing the pooled population of subsets of particles to the sample, and wherein exposing the proteins to the first detection reagent comprises adding the first detection reagent to the exposed pooled population.

4. The method of claim **3**, comprising washing the exposed pooled population prior to adding the first detection reagent.

5. The method of claim **1**, wherein the first posttranslational modification is phosphorylation.

6. The method of claim **5**, wherein the first posttranslational modification is phosphorylation of a serine, threonine or tyrosine residue, or a combination thereof.

7. The method of claim **1**, wherein the first posttranslational modification is ubiquitination, sumoylation, glycosylation, prenylation, myristoylation, farnesylation or acetylation.

8. The method of claim **1**, wherein the particles are microspheres.

9. The method of claim **8**, wherein the microspheres of each subset are distinguishable from those of the other subsets on the basis of their fluorescent emission spectra, their diameter, or a combination thereof.

10. The method of claim **1**, wherein the capture reagent comprises one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, a synthetic peptide, a substrate analog or a ligand.

11. The method of claim **1**, wherein the first detection reagent comprises one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, or a synthetic peptide.

12. The method of claim **1**, wherein the first detection reagent is an antibody specific for a phosphorylated tyrosine, serine or threonine residue, or a combination thereof.

13. The method of claim **1**, wherein the first detection reagent is an antibody specific for ubiquitin, an antibody specific for a carbohydrate moiety or an antibody specific for an acetyl group.

14. The method of claim **1**, wherein the first detection reagent comprises a first fluorescent label, and wherein detecting the presence or absence of the first detection reagent comprises detecting a first fluorescent signal from the first label.

15. The method of claim **1**, wherein detecting the presence or absence of the first detection reagent comprises: adding a labeled secondary agent that binds the first detection reagent and detecting a signal from the labeled secondary agent.

16. The method of claim **1**, wherein the proteins comprise one or more of: an endogenous cellular protein or a protein encoded by an infectious agent.

17. The method of claim **1**, wherein the plurality of proteins comprises a plurality of protein kinases.

18. The method of claim **1**, wherein the sample is derived from an animal, a human, a plant, a cultured cell or a microorganism.

19. The method of claim **1**, wherein the sample comprises one or more of: a cell lysate, an intercellular fluid, a conditioned culture medium or a bodily fluid.

20. The method of claim **1**, wherein the sample is derived from a tissue, a biopsy or a tumor.

21. The method of claim **1**, comprising recovering at least one of the subsets of particles.

22. The method of claim **1**, comprising:

providing a second detection reagent;

exposing the proteins to the second detection reagent; and,

detecting the presence or absence of the second detection reagent on each subset of particles.

23. The method of claim **22**, wherein the second detection reagent provides an indication of the presence of a second posttranslational modification.

24. A method of diagnosing or monitoring disease by detecting the presence or absence of a phosphorylated amino acid residue in a plurality of protein kinases, the method comprising:

providing a sample comprising the protein kinases;

providing a pooled population of a plurality of subsets of particles, the particles in each subset comprising a capture reagent specific for at least one of the kinases, and the particles in each subset being distinguishable from those of every other subset;

providing a single first detection reagent, the first detection reagent providing an indication of the presence of the phosphorylated amino acid residue;

binding the protein kinases to the capture reagents;

exposing the protein kinases to the first detection reagent;

generating a kinase activity profile for the sample by determining whether each of the kinases comprises the phosphorylated amino acid residue by identifying each subset of particles and detecting the presence or absence of the first detection reagent on each subset of particles; and,

comparing the kinase activity profile for the sample with one or more control kinase activity profiles.

25. The method of claim **24**, wherein the particles in each subset comprise a capture reagent specific for one of the kinases.

26. The method of claim **24**, wherein binding the protein kinases to the capture reagents comprises exposing the pooled population of subsets of particles to the sample, and wherein exposing the protein kinases to the first detection reagent comprises adding the first detection reagent to the exposed pooled population.

27. The method of claim **26**, comprising washing the exposed pooled population prior to adding the first detection reagent.

28. The method of claim **24**, wherein the phosphorylated amino acid residue is a serine, threonine or tyrosine residue, or a combination thereof.

29. The method of claim **24**, wherein the particles are microspheres.

30. The method of claim **29**, wherein the microspheres of each subset are distinguishable from those of the other subsets on the basis of their fluorescent emission spectra, their diameter, or a combination thereof.

31. The method of claim **24**, wherein the capture reagents are antibodies.

32. The method of claim **24**, wherein the first detection reagent comprises one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein or a synthetic peptide.

33. The method of claim **24**, wherein the first detection reagent is an antibody specific for a phosphorylated tyrosine, serine or threonine residue, or a combination thereof.

34. The method of claim **24**, wherein the first detection reagent comprises a fluorescent label, and wherein detecting the presence or absence of the first detection reagent comprises detecting a fluorescent signal from the label.

35. The method of claim **24**, wherein detecting the presence or absence of the first detection reagent comprises: adding a labeled secondary agent that binds the first detection reagent and detecting a signal from the labeled secondary agent.

36. The method of claim **24**, wherein the kinases comprise one or more of: an endogenous cellular protein or a protein encoded by an infectious agent.

37. The method of claim **24**, wherein the sample is derived from an animal, a human or a plant.

38. The method of claim **24**, wherein the sample comprises a cell lysate.

39. The method of claim **24**, wherein the sample is derived from a tissue, a biopsy or a tumor.

40. The method of claim **24**, wherein the control kinase activity profiles comprise one or more of: a kinase activity profile for a normal, healthy cell; a kinase activity profile for a diseased cell; or a kinase activity profile for a second sample from the same source, taken at a different time.

41. The method of claim **24**, comprising recovering at least one of the subsets of particles.

42. The method of claim **24**, comprising:

providing a second detection reagent;

exposing the protein kinases to the second detection reagent; and,

detecting the presence or absence of the second detection reagent on each subset of particles.

43. A method of detecting the presence or absence of one or more nucleic acid binding proteins, the method comprising:

providing a sample comprising or suspected of comprising the one or more nucleic acid binding proteins;

providing one or more subsets of particles, the particles in each subset comprising a nucleic acid binding site specific for at least one of the proteins, and the particles in each subset being distinguishable from those of every other subset;

providing one or more detection reagents, each detection reagent providing an indication of the presence of at least one of the nucleic acid binding proteins;

exposing the one or more subsets of particles to the sample and then adding the one or more detection reagents to the exposed one or more subsets, or

adding the one or more detection reagents to the sample and then exposing the one or more detection reagents and the sample to the one or more subsets of particles; and,

determining whether each of the one or more proteins is present in the sample by identifying each subset of particles and detecting the presence or absence of the one or more detection reagents.

44. The method of claim **43**, wherein the particles in each subset comprise a nucleic acid binding site specific for one of the proteins.

45. The method of claim **43**, wherein the particles are microspheres.

46. The method of claim **45**, wherein the microspheres of each subset are distinguishable from those of the other subsets on the basis of their fluorescent emission spectra, their diameter, or a combination thereof.

47. The method of claim **43**, wherein the nucleic acid binding site comprises one or more of: single-stranded DNA, double-stranded DNA, single-stranded RNA or double-stranded RNA.

48. The method of claim **43**, wherein the one or more detection reagents comprise one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, a synthetic peptide, a ligand or a substrate analog.

49. The method of claim **48**, wherein the one or more detection reagents comprise one or more antibodies specific for one or more of the nucleic acid binding proteins.

50. The method of claim **43**, wherein the one or more detection reagents each comprise a first fluorescent label, and wherein detecting the presence or absence of the one or more detection reagents comprises detecting a first fluorescent signal from the first label.

51. The method of claim **43**, wherein detecting the presence or absence of the one or more detection reagents comprises: adding a labeled secondary agent that binds the one or more detection reagents and detecting a signal from the labeled secondary agent.

52. The method of claim **43**, wherein the nucleic acid binding proteins comprise one or more of: an endogenous cellular protein or a protein encoded by an infectious agent.

53. The method of claim **43**, comprising recovering at least one of the subsets of particles.

54. A method of detecting the presence or absence of a plurality of posttranslational modifications of a plurality of proteins in a sample, the method comprising:

providing the sample comprising the proteins;

providing a solid support comprising a plurality of capture reagents, each capture reagent specific for at least one of the proteins, and each capture reagent provided at a known, pre-determined position on the solid support;

providing a plurality of detection reagents, each detection reagent providing an indication of the presence of one of the posttranslational modifications;

binding the proteins to the capture reagents;

exposing the proteins to the detection reagents; and,

determining whether each of the proteins comprises each of the posttranslational modifications by detecting the presence or absence of each of the detection reagents.

55. The method of claim **54**, wherein each capture reagent is specific for one of the proteins.

56. The method of claim **54**, wherein binding the proteins to the capture reagents comprises exposing the support to the sample, and wherein exposing the proteins to the detection reagents comprises adding the detection reagents to the exposed support.

57. The method of claim **56**, comprising washing the exposed support prior to adding the detection reagents.

58. The method of claim **54**, wherein the solid support is a membrane, a plate, or a slide.

59. The method of claim **54**, wherein the posttranslational modifications comprise one or more of: ubiquitination; sumoylation; glycosylation; prenylation; myristoylation; farnesylation; acetylation; or phosphorylation of a serine, threonine or tyrosine residue.

60. The method of claim **54**, wherein the capture reagents comprise one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, a synthetic peptide, a ligand or a substrate analog.

61. The method of claim **54**, wherein the detection reagents comprise one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, or a synthetic peptide.

62. The method of claim **54**, wherein the detection reagents comprise one or more of: an antibody specific for a phosphorylated tyrosine, serine or threonine residue, or a combination thereof; an antibody specific for ubiquitin; an antibody specific for a carbohydrate moiety; or an antibody specific for an acetyl group.

63. The method of claim **54**, wherein each detection reagent comprises a fluorescent label emitting a distinct signal, and wherein detecting the presence or absence of the detection reagents comprises detecting the fluorescent signals from the labels.

64. A composition, comprising:

a plurality of subsets of particles, the particles in each subset comprising a capture reagent specific for at least one of a plurality of proteins comprising or suspected of comprising a first posttranslational modification, and the particles in each subset being distinguishable from those of every other subset; and,

a single first detection reagent, the first detection reagent providing an indication of the presence of the first posttranslational modification.

65. The composition of claim **64**, wherein the particles in each subset comprise a capture reagent specific for one of the plurality of proteins.

66. The composition of claim **64**, comprising the plurality of proteins comprising or suspected of comprising the first posttranslational modification.

67. The composition of claim **66**, wherein each of the plurality of proteins is associated with one of the subsets of particles.

68. The composition of claim **66**, wherein the proteins comprise one or more of: an endogenous cellular protein or a protein encoded by an infectious agent.

69. The composition of claim **66**, wherein the plurality of proteins comprises a plurality of protein kinases.

70. The composition of claim **64**, wherein the first posttranslational modification is phosphorylation of a serine, threonine or tyrosine residue, or a combination thereof.

71. The composition of claim **64**, wherein the first posttranslational modification is ubiquitination, sumoylation, glycosylation, prenylation, myristoylation, farnesylation or acetylation.

72. The composition of claim **64**, wherein the particles are microspheres.

73. The composition of claim **72**, wherein the microspheres of each subset are distinguishable from those of the other subsets on the basis of their fluorescent emission spectra, their diameter, or a combination thereof.

74. The composition of claim **64**, wherein the capture reagent comprises one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, a synthetic peptide, a substrate analog or a ligand.

75. The composition of claim **64**, wherein the first detection reagent comprises one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, or a synthetic peptide.

76. The composition of claim **64**, wherein the first detection reagent is an antibody specific for a phosphorylated tyrosine, serine or threonine residue, or a combination thereof.

77. The composition of claim **64**, wherein the first detection reagent is an antibody specific for ubiquitin, an antibody specific for a carbohydrate moiety, or an antibody specific for an acetyl group.

78. The composition of claim **64**, wherein the first detection reagent comprises a first fluorescent label.

79. The composition of claim **64**, comprising a labeled secondary agent that binds the first detection reagent.

80. The composition of claim **64**, comprising a second detection reagent.

81. The composition of claim **80**, wherein the second detection reagent provides an indication of the presence of a second posttranslational modification.

82. A system comprising the composition of claim **64** and one or more fluid or particle handling or fluid or particle containing elements.

83. A kit comprising each of the components of the composition of claim **64** and instructions for using the composition to detect at least one posttranslational modification, packaged in one or more containers.

84. A composition comprising one or more subsets of particles, the particles in each subset comprising a nucleic acid binding site specific for at least one nucleic acid binding protein, and the particles in each subset being distinguishable from those of every other subset.

85. The composition of claim **84**, wherein the particles in each subset comprise a nucleic acid binding site specific for one nucleic acid binding protein.

86. The composition of claim **84**, comprising one or more nucleic acid binding proteins.

87. The composition of claim **86**, wherein each nucleic acid binding protein is associated with one of the one or more subsets of particles.

88. The composition of claim **84**, comprising one or more detection reagents, each detection reagent providing an indication of the presence of at least one nucleic acid binding protein.

89. The composition of claim **88**, wherein the one or more detection reagents comprise one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, a synthetic peptide, a substrate analog or a ligand.

90. The composition of claim **89**, wherein the one or more detection reagents comprise one or more antibodies specific for one or more of the nucleic acid binding proteins.

91. The composition of claim **88**, wherein the one or more detection reagents each comprise a first fluorescent label.

92. The composition of claim **88**, comprising a labeled secondary agent that binds the one or more detection reagents

93. The composition of claim **84**, wherein the particles are microspheres.

94. The composition of claim **93**, wherein the microspheres of each subset are distinguishable from those of the other subsets on the basis of their fluorescent emission spectra, their diameter, or a combination thereof.

95. The composition of claim **84**, wherein the nucleic acid binding site comprises one or more of: single-stranded DNA, double-stranded DNA, single-stranded RNA or double-stranded RNA.

96. A system comprising the composition of claim **84** and one or more fluid or particle handling or fluid or particle containing elements.

97. A kit comprising each of the components of the composition of claim **84** and instructions for using the composition to detect at least one nucleic acid binding protein, packaged in one or more containers.

98. A composition, comprising:

a plurality of proteins comprising or suspected of comprising a plurality of posttranslational modifications;

a solid support comprising a plurality of capture reagents, each capture reagent specific for at least one of the proteins, and each capture reagent provided at a known, pre-determined position on the solid support; and,

a plurality of detection reagents, each detection reagent providing an indication of the presence of one of the posttranslational modifications.

99. The composition of claim **98**, wherein each capture reagent is specific for one of the proteins.

100. The composition of claim **98**, wherein the solid support is a membrane, a plate, or a slide.

101. The composition of claim **98**, wherein the posttranslational modifications comprise one or more of: ubiquitination; sumoylation; glycosylation; prenylation; myristoylation; farnesylation; acetylation; or phosphorylation of a serine, threonine or tyrosine residue.

102. The composition of claim **98**, wherein the capture reagents comprise one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, a synthetic peptide, a substrate analog or a ligand.

103. The composition of claim **98**, wherein the detection reagents comprise one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, or a synthetic peptide.

104. The composition of claim **98**, wherein the detection reagents comprise one or more of: an antibody specific for a phosphorylated tyrosine, serine or threonine residue, or a combination thereof; an antibody specific for ubiquitin; an antibody specific for a carbohydrate moiety; or an antibody specific for an acetyl group.

105. The composition of claim **98**, wherein each detection reagent comprises a fluorescent label emitting a distinct signal.

106. The composition of claim **98**, comprising one or more labeled secondary agents that bind the detection reagents.

107. A system comprising the composition of claim **98** and at least one detector.

108. A kit comprising each of the components of the composition of claim **98** and instructions for using the composition to detect a plurality of posttranslational modifications, packaged in one or more containers.

109. A kit for detecting the presence or absence of a first posttranslational modification of a plurality of proteins in a sample, comprising:

a plurality of subsets of particles, the particles in each subset being distinguishable from those of every other subset; and,

a single first detection reagent capable of providing an indication of the presence of the first posttranslational modification,

packaged in one or more containers.

110. The kit of claim **109,** wherein the particles in each subset comprise a capture reagent specific for at least one of the proteins.

111. The kit of claim **110,** wherein the capture reagent is specific for one of the proteins.

112. The kit of claim **110,** wherein the proteins are protein kinases and wherein each capture reagent is specific for one of the protein kinases.

113. The kit of claim **110,** wherein the capture reagent comprises one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, a synthetic peptide, a substrate analog or a ligand.

114. The kit of claim **109,** wherein the first posttranslational modification is phosphorylation of a serine, threonine or tyrosine residue, or a combination thereof.

115. The kit of claim **109,** wherein the first posttranslational modification is ubiquitination, sumoylation, glycosylation, prenylation, myristoylation, farnesylation or acetylation.

116. The kit of claim **109,** wherein the particles are microspheres.

117. The kit of claim **116,** wherein the microspheres of each subset are distinguishable from those of the other subsets on the basis of their fluorescent emission spectra, their diameter, or a combination thereof.

118. The kit of claim **109,** wherein the first detection reagent comprises one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, or a synthetic peptide.

119. The kit of claim **109,** wherein the first detection reagent is an antibody specific for a phosphorylated tyrosine, serine or threonine residue, or a combination thereof.

120. The kit of claim **109,** wherein the first detection reagent is an antibody specific for ubiquitin, an antibody specific for a carbohydrate moiety or an antibody specific for an acetyl group.

121. The kit of claim **109,** wherein the first detection reagent comprises a fluorescent label.

122. The kit of claim **109,** wherein the kit comprises a labeled secondary agent that binds the first detection reagent.

123. The kit of claim **109,** comprising a second detection reagent.

124. The kit of claim **123**, wherein the second detection reagent provides an indication of the presence of a second posttranslational modification.

125. The kit of claim **109,** comprising instructions for use of the kit.

126. The kit of claim **125**, wherein the instructions comprise: instructions for attaching a capture reagent to each subset of particles, if the capture reagent is not already attached; instructions for binding the proteins to the capture reagents; instructions for exposing the proteins to the first detection reagent; instructions for determining whether each of the proteins comprises the first posttranslational modification by identifying each subset of particles and detecting the presence or absence of the first detection reagent; or a combination thereof.

127. A kit for detecting the presence or absence of one or more nucleic acid binding proteins in a sample, comprising:

one or more subsets of particles, the particles in each subset being distinguishable from those of every other subset; and,

one or more detection reagents, each detection reagent providing an indication of the presence of at least one of the nucleic acid binding proteins,

packaged in one or more containers.

128. The kit of claim **127**, wherein the particles in each subset comprise a nucleic acid binding site specific for at least one of the nucleic acid binding proteins.

129. The kit of claim **128**, wherein the particles in each subset comprise a nucleic acid binding site specific for one of the nucleic acid binding proteins.

130. The kit of claim **128**, wherein the nucleic acid binding site comprises one or more of: single-stranded DNA, double-stranded DNA, single-stranded RNA or double-stranded RNA.

131. The kit of claim **127**, wherein the particles are microspheres.

132. The kit of claim **131**, wherein the microspheres of each subset are distinguishable from those of the other subsets on the basis of their fluorescent emission spectra, their diameter, or a combination thereof.

133. The kit of claim **127**, wherein the one or more detection reagents comprise one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, a synthetic peptide, a substrate analog or a ligand.

134. The kit of claim **127**, wherein the one or more detection reagents comprise one or more antibodies specific for one or more of the nucleic acid binding proteins.

135. The kit of claim **127**, wherein the one or more detection reagents each comprise a first fluorescent label.

136. The kit of claim **127**, comprising a labeled secondary agent that binds the one or more detection reagents

137. The kit of claim **127,** comprising instructions for use of the kit.

138. The kit of claim **137**, wherein the instructions comprise: instructions for attaching a nucleic acid binding site to each subset of particles, if the binding site is not already attached; instructions for exposing the one or more subsets of particles to the sample and adding the one or more detection reagents to the exposed subsets; instructions for determining whether each of the proteins is present in a sample by identifying each subset of particles and detecting the presence or absence of the one or more detection reagents; or a combination thereof.

139. A kit for detecting the presence or absence of a plurality of posttranslational modifications of a plurality of proteins in a sample, comprising:

a solid support comprising a plurality of capture reagents, each capture reagent specific for at least one of the proteins, and each capture reagent provided at a known, pre-determined position on the solid support; and,

a plurality of detection reagents, each detection reagent providing an indication of the presence of one of the posttranslational modifications,

packaged in one or more containers.

140. The kit of claim **139,** wherein each capture reagent is specific for one of the proteins.

141. The kit of claim **139,** wherein the capture reagents comprise one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, a synthetic peptide, a substrate analog or a ligand.

142. The kit of claim **139,** wherein the posttranslational modifications comprise one or more of: ubiquitination; sumoylation; glycosylation; prenylation; myristoylation; farnesylation; acetylation; or phosphorylation of a serine, threonine or tyrosine residue.

143. The kit of claim **139,** wherein the detection reagents comprise one or more of: a nucleic acid, an oligonucleotide, a polypeptide, an antibody, a recombinant protein, or a synthetic peptide.

144. The kit of claim **139,** wherein the detection reagents comprise one or more of: an antibody specific for ubiquitin; an antibody specific for a carbohydrate moiety; an antibody specific for an acetyl group; or an antibody specific for a phosphorylated tyrosine, serine or threonine residue, or a combination thereof.

145. The kit of claim **139,** wherein each detection reagent comprises a distinct fluorescent label.

146. The kit of claim **139,** wherein the kit comprises one or more labeled secondary agents that bind the first detection reagents.

147. The kit of claim **139,** comprising instructions for use of the kit.

148. The kit of claim **147**, wherein the instructions comprise: instructions for binding the proteins to the capture reagents; instructions for exposing the proteins to the detection reagents; instructions for determining whether each of the proteins comprises the posttranslational modifications by identifying each position on the support and detecting the presence or absence of each detection reagent; or a combination thereof.